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Amendments

Claim 1 (Previously Presented): A compound having the formula (I):

$$R^{1}$$
 R^{2}
 R^{3}
 R^{4}
 R^{4}
 R^{28}
 R^{7}
 R^{11}
 R^{10}
 R^{10}
 R^{10}
 R^{10}
 R^{10}

or a pharmaceutically acceptable salt or solvate thereof, wherein

 Ar^1 and Ar^2 are each independently selected from the group consisting of $(R^{19})_{n7}$ -heteroaryl- and

 X^1 is selected from the group consisting of -O-, -S-, -SO-, -SO₂-, -NR¹²-, -N(COR¹²)- and -N(SO₂R¹⁵)-;

 R^1 , R^3 and R^5 are each independently selected from the group consisting of H and $C_1\text{-}C_6$ alkyl;

 R^2 , R^4 and R^6 are each independently selected from the group consisting of H, -CONR¹³R¹⁴ and -(CH₂)_{n1}-G; wherein G is selected from the group consisting of H, -CF₃, -CHF₂, -CH₂F, -OH, -O-(C₁-C₆)alkyl, -SO₂R¹³, -O-(C₃-C₈ cycloalkyl), -NR¹³R¹⁴, -SO₂NR¹³R¹⁴, -NR¹³SO₂R¹⁵, -NR¹³COR¹², -NR¹²(CONR¹³R¹⁴), -CONR¹³R¹⁴, -COOR¹² and C₃-C₈ cycloalkyl; or

 R^1 and R^2 , taken together with the carbon to which they are attached, form a $C_3\text{-}C_6$ cycloalkyl ring; or

R¹ and R², taken together with the carbon to which they are attached, form a

group; or

R³ and R⁴, taken together with the carbon to which they are attached, form a

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group; or

R⁵ and R⁶, taken together with the carbon to which they are attached, form a

₹ 0 ₹ 0 ₹ 0 ₹ 0

group;

 R^7 and R^{11} are each independently selected from the group consisting of H, C_1 - C_6 alkyl, C_3 - C_8 cycloalkyl, $(R^{16})_{n7}$ -aryl-, $(R^{19})_{n7}$ -heteroaryl-, -COOR²⁹, -CONR²¹R²², -CON(R^{21})(CH₂)_n- G^1 , -S(O)_{n5}(CH₂)_n- G^1 , -S(O)_{n5}R¹³, -CO(CH₂)_n- G^1 and -(CH₂)_{n1}- G^1 ; wherein

n is 0-4, and

 $G^{1} \text{ is selected from the group consisting of H, -OH, } (C_{1}\text{-}C_{6}) \text{alkyl}, \\ -O\text{-}(C_{1}\text{-}C_{6} \text{ alkyl}), -S(O)_{n5}R^{13}, -O\text{-}(C_{3}\text{-}C_{8} \text{ cycloalkyl}), -NR^{13}R^{14}, \\ -SO_{2}NR^{13}R^{14}, -NR^{13}SO_{2}R^{15}, -NR^{13}COR^{12}, -NR^{12}(CONR^{13}R^{14}), \\ -OC(=O)R^{12}, -CONR^{13}R^{14}, -COOR^{12}, C_{3}\text{-}C_{8} \text{ cycloalkyl, -CF}_{3}, \\ (R^{16})_{n7}\text{-aryl-O-, } (R^{16})_{n7}\text{-aryl-, } (R^{19})_{n7}\text{-heteroaryl-, } \\ (R^{19})_{n7}\text{-heterocycloalkyl- and alkenyl, and}$

provided that, when n is 0, then G^1 is selected from the group consisting of H, (C_1-C_6) alkyl, alkenyl, -CONR¹³R¹⁴, -COOR¹², C_3-C_8 cycloalkyl, -CF₃, $(R^{16})_{n7}$ -aryl-, $(R^{19})_{n7}$ -heteroaryl-, and $(R^{19})_{n7}$ -heterocycloalkyl-; and

provided that, when n_1 is 1, then G^1 is selected from the group consisting of H, $(C_1\text{-}C_6)$ alkyl, alkenyl, $-S(O)_{n5}R^{13}$, $-SO_2NR^{13}R^{14}$, $-CONR^{13}R^{14}$, $-COOR^{12}$, $C_3\text{-}C_8$ cycloalkyl, $-CF_3$, $(R^{16})_{n7}$ -aryl-, $(R^{19})_{n7}$ -heteroaryl- wherein said heteroaryl ring is bound by a ring carbon to the $-(CH_2)_{n1}$ - group, and $(R^{19})_{n7}$ -heterocycloalkyl- wherein said heterocycloalkyl ring is bound by a ring carbon to the $-(CH_2)_{n1}$ - group; or

R⁷ and R¹¹, taken together with the nitrogen to which they are attached, form a 5-7 membered heterocycloalkyl ring of the following formula:

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R⁷ and R¹¹, taken together with the nitrogen to which they are attached, form a 5-membered ring having the formula (A) or (B):

$$\begin{array}{cccc}
A & & & & & & \\
N & & & & & & \\
N-N & & & & & & \\
N-N & & & & & & \\
N-NH & & & & & & \\
(A) & & & & & (B)
\end{array}$$

X is selected from the group consisting of $-NR^{20}$ -, $-N(CONR^{13}R^{14})$ -, $-N(CO_2R^{13})$ -, $-N(SO_2R^{15})$ -, $-N(COR^{12})$ -, $-N(SO_2NHR^{13})$ -, -O-, -S-, -SO-, $-SO_2$ -, $-CF_2$ -, $-CH_2$ -, and $-C(R^{12})F$ -;

 R^8 , R^9 and R^{10} are each independently selected from the group consisting of H, C_1 - C_6 alkyl, C_3 - C_8 cycloalkyl, $-OR^{12}$, halogen, -CN, -NO₂, -CF₃, -CHF₂, -CH₂F, -OCF₃, -OCH₂F, -COOR¹², -CONR²¹R²², -NR²¹COR¹², -NR²¹CO₂R¹⁵, -NR²¹CONR²¹R²², -NR²¹CONR²¹R²², -NR²¹CONR²¹R²², -S(O)_{n5}R¹⁵, (R¹⁶)_{n7}-aryland (R¹⁹)_{n7}-heteroaryl-;

 R^{12} is selected from the group consisting of H, C_1 - C_6 alkyl and C_3 - C_8 cycloalkyl;

 R^{13} and R^{14} are each independently selected from the group consisting of H, C_1 - C_6 alkyl, C_2 - C_3 alkyl-O-CH₃, C_3 - C_8 cycloalkyl, $(R^{19})_{n7}$ -aryl(CH₂)_{n6}- and $(R^{19})_{n7}$ -heteroaryl-(CH₂)_{n6}-; or

R¹³ and R¹⁴, taken together with the nitrogen to which they are attached, form a 4-7 membered ring containing from 0-3 additional heteroatoms selected from the group consisting of –O-, -S- and –NR¹²-;

R¹⁵ is C₁-C₆ alkyl, C₃-C₈ cycloalkyl or -CF₃;

R¹⁶ is 1 to 3 substituents each independently selected from the group consisting of C₁-C₆ alkyl, C₃-C₈ cycloalkyl, C₁-C₆ alkoxy, halogen and –CF₃;

R¹⁹ is 1 to 3 substituents each independently selected from the group consisting of C₁-C₆ alkyl, C₃-C₈ cycloalkyl, -OH, halogen, -CN, -NO₂, -C(O)CF₃, -CF₃, -CH₂F, -OCF₃, -OCH₂F, -OCH₂F, -O-(C₁-C₆ alkyl), -O-(C₃-C₈ cycloalkyl),

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-COOR¹², -CONR²¹R²², -NR²¹R²², -NR²¹COR¹², -NR²¹CO₂R¹², -NR²¹CONR²¹R²², -NR²¹SO₂R¹⁵ and -S(O)_{n5}R¹⁵;

R²⁰ is H, C₁-C₆ alkyl, C₃-C₈ cycloalkyl, -(CH₂)_{n6}-heterocycloalkyl,

 $(R^{19})_{n7}$ -aryl(CH₂)_{n6}- or $(R^{19})_{n7}$ -heteroaryl-(CH₂)_{n6}-;

 R^{21} and R^{22} are each independently selected from the group consisting of H, C_1 - C_6 alkyl, C_3 - C_8 cycloalkyl and benzyl; or

R²¹ and R²², taken together with the nitrogen to which they are attached, form a 4-7 membered heteroaryl ring containing from 0-3 additional heteroatoms selected from the group consisting of –O-, -S- and –NR¹²-;

 R^{23} and R^{24} are each independently selected from the group consisting of H, C_1 - C_6 alkyl and $-CONR^{13}R^{14}$; or

R²³ and R²⁴, taken together with the carbon atom to which they are attached, form a

group;

 R^{25} , R^{26} , R^{27} and R^{28} are each independently selected from the group consisting of H and C_{1} – C_{6} alkyl; or

R²⁵ and R²⁶, taken together with the carbon atom to which they are attached, form a

group; or

R²⁷ and R²⁸, taken together with the carbon atom to which they are attached, form a

group;

R²⁹ is selected from the group consisting of C₁-C₆ alkyl and C₃-C₈ cycloalkyl;

n₁ is 1-4;

n₄ is 0-2;

n₅ is 0-2;

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n₆ is 0-3;

n₇ is 0-3; and

provided that, when n_4 is 0, and R^{25} and R^{26} are each H, then X is not –O-, -NR²⁰- or –S-.

Claim 2 (Original): The compound of Claim 1 wherein X1 is -O-.

Claim 3 (Original): The compound of Claim 1 wherein Ar¹ and Ar² are each independently

Claim 4 (Original): The compound of Claim 3 wherein R⁸, R⁹ and R¹⁰ are each independently selected from the group consisting of H, -CH₃, halogen and -CF₃.

Claim 5 (Original): The compound of Claim 1 wherein

X1 is -O-; and

Ar1 and Ar2 are each independently

wherein R^8 , R^9 and R^{10} are each independently selected from the group consisting of H, -CH₃, halogen and -CF₃.

Claim 6 (Original): The compound of Claim 1 wherein

Ar² is

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wherein,

R⁸ is selected from the group consisting of H and F, and R⁹ and R¹⁰ are each independently selected from the group consisting of H, - CH₃, F, CI and -CF₃.

Claim 7 (Original): The compound of Claim 6 wherein X¹ is -O-; and R²⁸ are each H.

Claim 8 (Original): The compound of Claim 6 wherein R⁵ and R⁶ are H.

Claim 9 (Original): The compound of Claim 7 wherein R⁷ and R¹¹, taken together with the nitrogen to which they are attached, form a 5-7 membered ring having the following formula:

$$R^{5}$$
 R^{6}
 R^{25}
 R^{26}
 R^{26}

Claim 10 (Original): The compound of Claim 1 having the formula

wherein R⁷, R⁸ and R¹¹ are selected from the group consisting of:

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R ⁸	R ⁷	R ¹¹
н	Н	Н
Н	Н	74
H	Н	
Н	Н	F F O
Н	Н	7-4-0
Н	H	7
Н	Н	٠, ٢, ١
Н	Н	4
Н	H	7. ON
H·	H	0 N
Н	Н	, NO.
н	Н	s 0

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4000	l	
н	н	
Н	, H	OH OH
Н	Н	
н	Н	L C L
Н	Н	F ₃ C
Н	. H	Z = 0
н	H	
Н	Н	7 19
н	H	
Н	Н	
н	Н	

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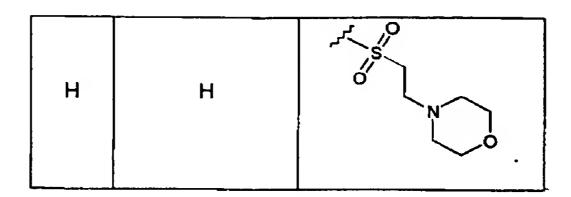
		
Н	н	
Н	Н	~~\\\\\\\\\\\\\\\\\\\\\\\\\\\\\\\\\\\\
Н	H	44 - 15 - 15 - 15 - 15 - 15 - 15 - 15 -
Н	Н	\(\frac{0}{1}\)
Н	н	r√ NH ₂
Н	-0 ¹ -7-1	N. C. N.
Н	S N	pre O-N
F	Н	4 4
F	H	Н
F	Н	ZZZ F F
F	Н	
F	Н	

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F	Н	*\f\\\\\\\\\\\\\\\\\\\\\\\\\\\\\\\\\\\
F	Н	٧٠ ()
F	Н	25 N
F	Н	
Н	Н	NH ₂
Н	Н	Jrt NH₂ O O
F	Н	rr NH₂
F	Н	NH ₂
Н	Н	Jr NH₂ O
Н	Н	7. 10 N
Н	Н	H N

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Claim 11 (Original): The compound of Claim 1 having the formula:

wherein R^1 , R^2 , R^7 , R^8 and R^{11} are selected from the group consisting of:

R ⁸	R ¹	R ²	-NR ⁷ R ¹¹
Н	Н	Н	O N O
н	Н	Н	N O
Н	Н	Н	
н	Н	Н	NH O
F	H	Н	

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F	Н	Н	
F	Н	н	N O
Н	Н	н	O THE O
Н	Н	СН₃	N O
Н	Н	CH₂OH	
Н	Н	Н	H ₂ N O
н	Н	Н	
Н	Н	н	
 Н	н	Н	N O
Н	Н	H	

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Н	Н	Н	2 2 2 2 2 2 2 2 2 2 2 2 2 2 2 2 2 2 2
Н	н	Н	HZ Z Z

Claim 12 (Original): The compound of Claim 11 or the pharmaceutically acceptable salt or solvate thereof, wherein R¹, R², R⁷ R⁸ and R¹¹ are selected from the group consisting of

R ⁸	R ¹	R ²	-NR ⁷ R ¹¹
Н	Н	Н	O N O
Н	Н	Н	N O NH
Н	H	CH₃	~j~ _N_O
Н	Н	СН₂ОН	~j^ _N_O
Н	H	Н	N-NH.

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Claim 13 (Original): The compound of Claim 12 having the formula:

Claim 14 (Original): The compound of Claim 12 having the formula:

Claim 15 (Original): The compound of Claim 12 having the formula:

Claim 16 (Original): The compound of Claim 12 having the formula:

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Claim 17 (Original): The compound of Claim 12 having the formula:

Claim 18 (Previously Presented): A pharmaceutical composition comprising a therapeutically effective amount of at least one compound of Claim 1, and a pharmaceutically acceptable carrier.

Claim 19 (Canceled).

Claim 20 (Withdrawn): A method for treating a physiological disorder, symptom or disease in a patient in need of such treatment, comprising administering to said patient an effective amount of at least one compound of Claim 1, wherein said physiological disorder, symptom or disease is selected from the group consisting of: respiratory diseases, inflammatory diseases, skin disorders, ophthalmalogical disorders, central nervous system conditions, addictions, epilepsy, nociception, psychosis, schizophrenia, Alzheimer's disease, AIDs related dementia, Towne's disease, stress related disorders, obsessive/compulsive disorders, eating disorders, sleep disorders, mania, premenstrual syndrome, gastrointestinal

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disorders, atherosclerosis, fibrosing disorders, obesity, Type II diabetes, pain related disorders, bladder and genitourinary disorders, and nausea.

Claim 21 (Withdrawn): A method for treating a physiological disorder, symptom or disease in a patient in need of such treatment, comprising administering to said patient an effective amount of at least one compound of Claim 1, wherein said physiological disorder, symptom or disease is selected from the group consisting of: a respiratory disease, depression, anxiety, phobia, bipolar disorder, alcohol dependence, psychoactive substance abuse, nociception, psychosis, schizophrenia, stress related disorder, obsessive/compulsive disorder, bulemia, anorexia nervosa, binge eating, sleep disorder, mania, premenstrual syndrome, gastrointestinal disorder, obesity, headache, neuropathic pain, post-operative pain, chronic pain syndrome, bladder disorder, genitourinary disorder, cough, emesis and nausea.

Claim 22 (Withdrawn): A method for treating a physiological disorder, symptom or disease in a patient in need of such treatment, comprising administering to said patient an effective amount of at least one compound of Claim 1, and an effective amount of at least one active ingredient selected from the group consisting of: other NK₁ receptor antagonists, selective serotonin reuptake inhibitors, dopamine receptor agonists, serotonin 5-HT₃ receptor antagonists, serotonin 5-HT_{2c} receptor agonists, nociceptin receptor agonists, glucocorticoids and inhibitors of multidrug resistance protein 5, wherein said physiological disorder, symptom or disease is selected from the group consisting of: a respiratory disease, depression, anxiety, phobia, bipolar disorder, alcohol dependence, psychoactive substance abuse, nociception, psychosis, schizophrenia, stress related disorder, obsessive/compulsive disorder, bulemia, anorexia nervosa, binge eating, sleep disorder, mania, premenstrual syndrome, gastrointestinal disorder, obesity, headache, neuropathic pain, post-operative pain, chronic pain syndrome, bladder disorder, genitourinary disorder, cough, emesis and nausea.

Claim 23 (Currently Amended): A method of treating emesis and/or nausea in a patient in need of such treatment comprising administering to said patient an 54627-1

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effective amount of at least one compound having the formula (I)of Claim 1 in combination with an effective amount of at least one serotonin 5-HT₃ receptor antagonist and/or at least one glucocorticoid.

Claim 24 (Withdrawn): The method of Claim 23 wherein said serotonin 5-HT₃ receptor antagonist is ondansetron and said glucocorticoid is dexamethasone.

Claim 25 (Withdrawn): The method of Claim 21, wherein the physiological disorder, symptom or disease is emesis, depression, anxiety or cough.

Claim 26 (Withdrawn): The method of Claim 25 wherein the physiological disorder, symptom or disease is depression or anxiety.

Claim 27 (Withdrawn): The method of Claim 26, further comprising administering to the patient an effective amount of at least one anti-depressant agent and/or at least one anti-anxiety agent.

Claim 28 (Withdrawn): The method of Claim 25 wherein depression is being treated and said method further comprises administering to the patient an effective amount of at least one selective serotonin reuptake inhibitor.

Claim 29 (Withdrawn): A method for antagonizing an effect of a Substance P at a neurokinin-1 receptor site or for blocking at least one neurokinin-1 receptor, in a patient in need of such treatment, comprising administering to said patient an effective amount of at least one compound of Claim 1.

Claims 30-35 (Canceled).